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  *                Help Desk --> 703-305-9000                     *
  *                                                               *
  *    The Help Desk is staffed for APS support 7 days/week.      *
  *      Monday through Friday:      6:30am - 9:00pm              *
  *      Saturday, Sunday, Holidays: 8:30am - 5:00 pm             *
  *                                                               *
  *    The Help Desk staff at this number will handle all APS     *
  *    related questions.                                         *
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  *    >>>>>>>>>>>>> NEW SUNDAY HOURS !!! <<<<<<<<<<<<<           *
  *                                                               *
  *    The APS is available:                                      *
  *            6:30am - 9:00pm Monday through Friday              *
  *            7:30am - 5:00pm Saturday, Sunday, Holidays         *
  *                                                               *
  *      APS is unavailable Thanksgiving Day, Christmas Day,      *
  *      and New Year's Day.                                      *
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  *              W E L C O M E   T O   T H E                      *
  *         U. S.   P A T E N T   T E X T   F I L E               *
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=> s diabet#(10n)(obese or obesity or weight(w)gain or over(w)eating)

            48 DIABET#
          1231 OBESE
          2309 OBESITY
        757474 WEIGHT
        140536 GAIN
       1420220 OVER
          7365 EATING
L1           1 DIABET#(10A)(OBESE OR OBESITY OR WEIGHT(W)GAIN OR OVER(W)EA
TIN
               G)

=> d l1 ti in fd ccls ab


US PAT NO:      4,698,419 [IMAGE AVAILABLE]            L1: 1 of 1
TITLE:          Hexapeptide
INVENTOR:       Evgeny I. Chazov, Moscow, Soviet Union
                Vladimir N. Smirnov, Moscow, Soviet Union
                Valentin A. Vinogradov, Moscow, Soviet Union
                Vladimir M. Polonsky, Moscow, Soviet Union
                Valentina A. Tischenko, Moscow, Soviet Union
                Mikhail I. Titov, Moscow, Soviet Union
                Zhanna D. Bespalova, Moscow, Soviet Union
                Boris L. Pekelis, Moscow, Soviet Union
DATE FILED:     Feb. 5, 1986
US-CL-CURRENT: 530/329; 930/10, 21, DIG.802

ABSTRACT:

 A novel hexapeptide having the following structure:
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Phe-Ala-Gly-Phe-Gly-Arg.
The hexapeptide according to the present invention has a hepatoprotective effect.

=> d l1 all

4,698,419 [IMAGE AVAILABLE] Oct. 6, 1987 L1: 1 of 1
Hexapeptide

INVENTOR: Evgeny I. Chazov, Moscow, Soviet Union
Vladimir N. Smirnov, Moscow, Soviet Union
Valentin A. Vinogradov, Moscow, Soviet Union
Vladimir M. Polonsky, Moscow, Soviet Union
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ASSIGNEE: Vsesojuzny Kardiologichesky Nauchny Tsentr Akademii Meditsinskikh Nauk SSSR, Moscow, Soviet Union (foreign corp.)

APPL-NO: 06/835,114
DATE FILED: Feb. 5, 1986
PCT-FILED: Apr. 24, 1985
PCT-NO: PCT/SU85/00031
371-DATE: Feb. 5, 1986
102(E)-DATE: Feb. 5, 1986
PCT-PUB-NO: WO86/00621
PCT-PUB-DATE: Jan. 30, 1986
FRN-PRIOR: Soviet Union 3772913 Jul. 16, 1984
INT-CL: [4] C07K 7/06
US-CL-ISSUED: 530/329
US-CL-CURRENT: 530/329; 930/10, 21, DIG.802
SEARCH-FLD: 530/329

REF-CITED:

U.S. PATENT DOCUMENTS

4,428,941	1/1984	Calibert et al.	530/329
4,578,217	3/1986	Vnek et al.	530/329

OTHER PUBLICATIONS

Article: Assessment of Antienzymatic Therapy of Destructive Pancreatitis, Yu A. Nesterenko; Yu P. Atanov.

ART-UNIT: 153
PRIM-EXMR: Delbert R. Phillips
LEGAL-REP: Ladas & Parry

ABSTRACT:

A novel hexapeptide having the following structure:

Phe-Ala-Gly-Phe-Gly-Arg.
The hexapeptide according to the present invention has a hepatoprotective effect.

1 Claims, 1 Drawing Figures
EXMPL-CLAIM: 1
NO-PP-DRAWING: 1

SUMMARY:

FIELD OF THE INVENTION

The present invention relates to the organic chemistry and, more particularly, to a novel hexapeptide.

BACKGROUND OF THE INVENTION

At the present time for the treatment of acute viral hepatitis, aggravation of chronic hepatitis and hepatocirrhosis synthetic glucocorticoidal hormonal preparations such as prednisolone and the like are most widely administered. These preparations are employed, as a rule, over long periods and cause a great number of complications on the part of various organs and systems. Glucocorticoids bring about atrophy of the cortical layer of adrenal glands, increased arterial pressure, development of steroid **diabets**, **obesity**, retention of urine, electrolytical disturbances, osteoporosis phenomena, pahological bone fractures. In the gastro-intestinal tract glucocorticoids frequently cause the formation of ulcers complicated with hemorrhages which provides an especially detrimental effect on the progress of chronic liver diseases. An abrupt cancellation of glucocorticoids results in the development of an acute adrenal insufficiency. Remissions in the treatment with preparations of this class are instable and of short duration. (cf. Scott J., Physiological pharmacological and pathological effects of glucocorticoids on the digestive system, Clin. gastroenterol.m 1981, v. 10, p. 627-652).

Known in the art are hexapeptides of a different structure, for example hexapeptide His-D-Trp-Ala-Trp-D-Phe-Lys-NH.sub.2 (Bowers Cy et al., Endocrinology, 1984, v. 114, No. 5, p. 1537-1545) or hexapeptide Tyr-D-Ala-Gly-Phe-Leu-Arg and the like (cf. A. V. Waldman, O. S. Medvedev. Theoretical Prerequisits for Finding New Cardio-Vascular Agents Among Peptides, "Vestnik Akademii Meditsinskikh Nauk SSSR", 1982, No. 5, p. 14-22).

However, the hepatoprotective activity of such compounds is hitherto unknown in the art.

DISCLOSURE OF THE INVENTION

The hexapeptide according to the present invention is novel and hitherto unknown in the literature.

The present invention is directed to the provision of a novel compound-hexapeptide exhibiting a high hepatoprotective activity, causing no side responses and useful in medicine.

This object is accomplished by a novel hexapeptide which, according to the present invention has the following structure: Phe-Ala-Gly-Phe-Gly-Arg

The hexapeptide according to the present invention comprises a white powder well soluble in distilled water, physiological solution, ethanol, insoluble in ether, ethylacetate, benzene. Melting point is 154.degree.-156.degree. C., (.alpha.).sub.D.sup.25 =+8.4 (with 0.5 H.sub.2 O).

DETDESC:

BEST MODE FOR CARRYING OUT THE INVENTION

The study of a hepatoprotective effect of the hexapeptide according to the present invention was carried out in comparison with prednisolone on male mice of the line Balb C.

The development of acute hepatitis was induced in mice subjected to a 12-hours' starving by means of D-galactosamine hydrochloride which was administered intraperitoneally diluted in 0.1 ml of a physiological solution in the dose of 700 mg/kg. The control group of animals was administered intraperitoneally with 0.1 ml of a physiological solution. The animals given D-galactosoamine hydrochloride were injected,

immediately after i[redacted] administration, with the hexap[redacted]tide according to the present inventi[redacted] (100 .mu.g/kg), prednisolone [redacted]ng/kg) or a physiological solution (0.1 ml) hypodermally. Repeated injections of the test preparations were made after 6 hours. Each of the groups consisted of 12 animals. The mice were slaughtered by decapitation, blood was collected and in its plasma concentrations of alanine transaminase and glutametedehydrogenase were determined.

The statistical processing of the results obtained was effected using t-criterion. The certain value was regarded as the dirrerence at the level of 95% (at P<0.05).

The results thus obtained are shown in Table 1.

TABLE 1

No.	Groups of animals	Concentration of alanine transaminase, JU/e	Concentration of glutamatede-hydrogenase, JU/e
1.	Control	113.6 .+-. 5.5	32.5 .+-. 3.8
2.	D-galactosamine hydrochloride + physiological solution	170.8 .+-. 10.1*	121.6 .+-. 16.0*
3.	D-galactosamine hydrochloride + hexapeptide of this invention	115.4 .+-. 5.2	**62.8 .+-. 4.9**
4.	D-galactosamine hydrochloride + prednisolone	151.2 .+-. 14.3	104.5 .+-. 10.1

*The difference between Group 1 and Group 2 is certain

The difference between Group 2 and Group 2 is certain

As it follows from the above Table, D-galactosamine hydrochloride causes a substantial increase of concentrations of the studied enzymes in the blood plasma. In this case the concentration of alanine transaminase increased by 1.5 times and that of glutamatedehydrogenase--by more that 3 times. The hexapeptide according to the present invention substantially fully blocked the increase of concentrations of alanine transaminase and reduced by 2 times the concentration of glutamatedehydrogenase. In the case of administration of prednisolone a trend was observed towards reducing the values of the studied parameters.

The hexapeptide according to the present invention was also studied on an experimental model of an acute liver injury in male rats of the V-star line induced by means of carbon tetrachloride. After a 12-hours' starvation the rats were given CCl.sub.4 in the concentration of 1 mg/kg diluted in olive oil intraperitoneally. After administration of CCl.sub.4 the rats were injected with the hexapeptide according to the present invention in different doses (10, 30, 100 and 300 .mu.g/kg). Repeated injections of the hexapeptide according to the invention were effected after 6, 24, and 30 hours. The control group of animals was given, instead of the hexapeptide of this invention, a physiological solution (0.2 ml). All the test groups of animals consisted of 13 rats. Concentrations of alanine transaminase and glutamatedehydrogenase were

determined in the rat's blood. The results obtained in these experiments are shown in the following Table 2.

TABLE 2

No.	Groups of animals	Concentration of alanine transaminase, JU/e	Concentration of glutamate-dehydrogenase, JU/e
1.	Vivarium control	64.6 .+-. 3.3	17.2 .+-. 0.6
2.	Carbon tetrachloride	4349.3 .+-. 2285.1	5619.7 .+-. 1201.7*
3.	CCl.sub.4 + hexapeptide of this invention (10 .mu.g/kg)	4141.5 .+-. 1094.8	1962.0 .+-. 494.7
4.	CCl.sub.4 + hexapeptide of this invention (30 .mu.g/kg)	3037.8 .+-. 580.8	1487.3 .+-. 301.5
5.	CCl.sub.4 + hexapeptide of this invention (100 .mu.g/kg)	2339.8 .+-. 333.4	874.3 .+-. 118.3
6.	CCl.sub.4 + hexapeptide of this invention (300 .mu.g/kg)	2110.1 .+-. 374.5	603.3 .+-. 118.0

*The difference with Group 1 is certain.
The difference with Group 2 is certain.

As it follows from Table 2 hereinabove, CCl.sub.4 causes a certain increase of a concentration of glutamatedehydrogenase. The increase of alanine transaminase is not statistically significant due to a small number of observations. The hexapeptide according to the present invention lowers both parameters depending on the dose. Especially pronounced is the reduction of a more specific hepatic enzyme-glutamatedehydrogenase.

The hexapeptide according to the present invention has also blocked lethality of rats in the case of using carbon tetrachloride. The results obtained are shown in Table 3. As it follows from this Table, while carbon tetrachloride causes death of 77% of the animals, administration of the hexapeptide according to the present invention in the doses of 100 and 300 .mu.g/kg no lethal cases are observed.

TABLE 3

Parameters	Dose of the hexapeptide of the invention (.mu.g/kg) 0	10	30	100	300
Number of rats survived after 48 hours	3	6	9	13	13

Lethal cases (%)	77	54	30*	0*	0*

*The difference from Group 0 is certain.

A statistical processing in the case of liver injury caused by carbon tetrachloride in respect of the enzymes was effected using t-criterion, while in respect of lethality--by means of .chi..sup.2 criterion.

In all of the experiments with the use of the hexapeptide according to the present invention no changes were observed on the part of the cell composition of the blood and basic hemohynamic characteristics. The acute toxicity of the hexapeptide according to the present invention LD.sub.50 was equal to 120 mg/kg.

The comparison of the hexapeptide of the present invention with somatostatin shows that the hexapeptide is superior over the latter in its efficiency: lethality of 0% as compared to 20% in the case of somatostatin; maximum effective dose is by 15 times lower (100 .mu.g/kg for the hexapeptide and 1.5 mg/kg for somatostatin).

Therefore, in the employed experimental models of an acute hepatitis the hexapeptide according to the present invention certainly lowered concentrations of glutamatedehydogenase and alanine transanimase in blood, the increase of which is characteristic for a pathological process developing in the liver. This points to the availability of hepatoprotective properties in the hexapeptide according to the present invention. Prednisolone when used in a conventionally employed parenteral dose does not provide any pronounced effect on the concentration of the enzymes.

The hexapeptide according to the present invention, as regards its activity, is superior to prednisolone (employed in a 50-times higher dose) and somatostatin (used in a 15-times greater dose). The hexapeptide according to the present invention, i.e. phenylalanyl-alanyl-glycyl-phenylalanyl-glycylarginine is synthesized by a method of a successive building-up of the aminoacid chain by one amino acid, starting from arginine as a free base and activated esters of protected amino acids by removing the protecting groups by way of a catalytical hydrogenolysis and an acidolytic cleavage.

For a better understanding of the present invention, the following example illustrating preparation of the hexapeptide according to the invention is given hereinbelow.

EXAMPLE 1

1.58 g (9.07 mN) of arginine are suspended in 25 ml of dimethylformamide, the solution is added with 3.30 g (9.98 mM) of p-nitrophenyl ester of carbobenzoxy glycin, the mixture is stirred at room temperature for one day. Dimethylformamide is evaporated, the residue is dissolved in 5 ml of methanol and added with 300 ml of ether. The resulting precipitate is filtered-off, washed in the filter with ether and dried in a vacuum desiccator.

There are thus obtained 3.09 g (93%) of carbobenzoxyglycyl-arginine with the melting point of 135.degree.-135.5.degree. C., [.alpha.].sub.D.sup.25 =+10.3 (CI, dimethylformamide).

R.sub.f.sup.I =0.25 (n-butanol:acetic acid:water 3:1:1) (A)

R.sub.f.sup.2 =0.54 (chloroform:methaol:32% acetic acid 60:45:20)(B)

R.sub.f.sup.3 =0.33 (ethylacetate:pyridine:acetic acid:water 45:20:5:11) (C).

3.09 g (8.46 mM) of carbobenzoxy-glycyl-arginine are dissolved in 35 ml of trifluoroacetic acid; a current of dry hydrogen bromide is passed through the resulting solution for one hour. The solvent is evaporated, the residue is added with 150 ml of ether; the resulting precipitate is filtered-off, dissolved in water and treated with an ion-exchange resin Amberlite IR A-410 (OH.sup.- form) to the negative reaction on bromine ions. The resin is filtered-off, washed in the filter with methanol and water; the filtrate is evaporated, the remaining water is removed by azeotropic distillation with isopropanol. The residue is dissolved in 25 ml of dimethylformamide, the solution is added with 3.91 g (9.21 mM) of p-nitrophenyl ester of carbobenzoxy-phenylalanine. The reaction mixture is maintained at room temperature for one day. Dimethylformamide is evaporated, the residue is dissolved in 5 ml of methanol and 300 ml of ether are added thereto. The resulting precipitate is filtered-off, washed with ester on the filter and dried in a vacuum desiccator. 3.75 g (86%) of carbobenzoxy-phenylalanyl-glycyl-arginine are thus obtained; melting point 133.degree.-134.degree. C., [.alpha.].sub.D.sup.25 =17.2 (cI, dimethylformamide), R.sub.f.sup.1 =0.30 (A), R.sub.f.sup.2 =0.66 (B), R.sub.f.sup.3 =0.43 (C).

Carbobenzoxy-glycyl-phenylalanyl-glycyl-arginine is prepared by the method similar to that described for the preparation of carbobenzoxy-phenylalanyl-glycyl-arginine on the basis of 2.71 g (5.28 mM) of the latter and 1.93 g (5.83 mM) of p-nitrophenyl ester of carbobenzoxy-glycin.

2.46 g (82%) of carbobenzoxy-glycyl-phenylalanyl-glycyl-arginine are obtained; melting point is 142.degree.-144.degree. C., [.alpha.].sub.D.sup.25 =-17.3 (CI, dimethylformamide); R.sub.f.sup.1 =0.57 (B), R.sub.f.sup.2 =0.35 (C), R.sub.f.sup.3 =0.45 (n-butanol:formic acid:water 15:3:1).

On the basis of 2.46 g (4.32 mM) of carbobenzoxy-glycyl-phenylalanyl-glycyl-arginine and 1.64 g (4.75 mM) of p-nitrophenyl ester of carbobenzoxyalanine in a manner similar to that described hereinbefore 2.13 g (77%) of carbobenzoxy-alanyl-glycyl-phenylalanyl-glycyl-arginine are obtained with the melting point of 148.degree.-149.degree. C., [.alpha.].sub.D.sup.25 =-20.8 (cI, dimethylformamide); R.sub.f.sup.1 =0.64 (B), R.sub.f.sup.2 =0.38 (C), R.sub.f.sup.3 =0.39 (n-butanol:pyridine:concentrated ammonia:water 20:12:3:15) (D).

From 0.64 g (0.99 mM) of carbobenzoxy-alanyl-glycyl-phenylalanyl-glycyl-arginine and 0.46 g (1.1 mM) of p-nitrophenyl ester of carbobenzoxyphenylalanine in a manner similar to that described hereinabove 0.63 g (81%) of carbobenzoxy-phenylalanyl-alanyl-glycyl-penylalanyl-glycyl-arginine is obtained; melting point is equal to 150.degree.-153.degree. C., [.alpha.].sub.D.sup.22 =-3.5 (cI, MeOH). R.sub.f.sup.1 =0.42 (A), R.sub.f.sup.2 =0.70 (B), R.sub.f.sup.3 =0.39 (C).

0.63 g (0.80 mM) of carbobenzoxy-phenylalanyl-alanyl-glycyl-phenylalanyl-glycyl-arginine is dissolved in 10 ml of methanol and hydrogenated in the presence of a palladium catalyst. The catalyst is filtered-off, washed on the filter with methanol, evaporated, the residue is reprecipitated with ester (100 ml) from methanol and dried in a vacuum desiccator. The resulting product is passed through a column (600.times.15) with Sephadex SP C-25 and fractioned in a gradient of a pyridineacetate buffer of 0.05-1.00 M.

0.34 g (65%) of phenylalanyl-alanyl-glycyl-phenylalanyl-glycyl-arginine is obtained; melting point is 154.degree.-156.degree. C.; [.alpha.].sub.D.sup.25 =+8.4 (c 0.5, H.sub.2 O); R.sub.f.sup.1 =0.58 (B), R.sub.f.sup.2 =0.32 (D), R.sub.f.sup.3 =0.44 (n-butanol:pyridine:acetic acid:water 10.5:5:1:7.5).

The amino acid analysis data:

Phenylalanine 2.13 (2), alanine 1.00 (1), glycine 1.97 (2), arginine 0.93 (I).

Individuality of the synthesized hexapeptide is proven by the NMR spectrum (FIG. 1) and by the method of a highly-effective gas-liquid chromatography. The peptide was eluted in one peack at 39.3% of the gradient on the 12.8-th minute.

(Column 250.times.4.6 mm, Spherisorb ODS, 5.mu.; mobile phase A; 0.05M KH.sub.2 PO.sub.4 ; pH 3.0; B:CH.sub.3 CN; gradient 20%.fwdarw.50% C for 20 minutes; pressure 1,500 psi; rate 1 mm/min; detection at 214 nm).

INDUSTRIAL APPLICABILITY

The hexapeptide according to the present invention exhibits a hepatoprotective effect and can be useful in medicine for the treatment of acute and chronic liver diseases.

CLAIMS:

We claim:

1. A hexapeptide of the following structure:

Phe-Ala-Gly-Phe-Gly-Arg.

```
=> s (obesity or obese or weight(w)gain or eating(w)disorder or
over(w)eating)(20n)diabet#

          2309 OBESITY
          1231 OBESE
        757474 WEIGHT
        140536 GAIN
          7365 EATING
         12793 DISORDER
       1420220 OVER
          7365 EATING
            48 DIABET#

L2             1 (OBESITY OR OBESE OR WEIGHT(W)GAIN OR EATING(W)DISORDER OR
OVE
                 R(W)EATING)(20A)DIABET#

=> s (obesity or obese or weight(w)gain or eating(w)disorder or
over(w)eating)(20n)(amylin or proamylin)

          2309 OBESITY
          1231 OBESE
        757474 WEIGHT
        140536 GAIN
          7365 EATING
         12793 DISORDER
       1420220 OVER
          7365 EATING
            85 AMYLIN
             6 PROAMYLIN

L3            18 (OBESITY OR OBESE OR WEIGHT(W)GAIN OR EATING(W)DISORDER OR
OVE
                 R(W)EATING)(20A)(AMYLIN OR PROAMYLIN)

=> d l3 ti in fd ccls ab 1-18
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US PAT NO: 5,795,861 [IMAGE AVAILABLE] L3: 1 of 18
TITLE: Methods for regulating gastrointestinal motility
INVENTOR: Orville G. Kolterman, Poway, CA
Timothy J. Rink, La Jolla, CA
DATE FILED: Jun. 5, 1995
US-CL-CURRENT: 514/12, 11, 13, 866; 530/307, 327

ABSTRACT:
Methods for treating conditions associated with elevated, inappropriate or undesired post-prandial blood glucose levels are disclosed which comprise administration of an effective amount of an amylin agonist alone or in conjunction with other anti-gastric emptying agents. Methods for reducing gastric motility and delaying gastric emptying for therapeutic and diagnostic purposes are also described.

US PAT NO: 5,759,551 [IMAGE AVAILABLE] L3: 2 of 18
TITLE: Immunogenic LHRH peptide constructs and synthetic universal immune stimulators for vaccines
INVENTOR: Anna Efim Ladd, Brooklyn, NY
Chang Yi Wang, Cold Spring Harbor, NY
Timothy Joseph Zamb, Stony Brook, NY
DATE FILED: Dec. 26, 1995
US-CL-CURRENT: 424/198.1, 185.1, 227.1; 514/841, 843

ABSTRACT:

This invention relates to immunogenic luteinizing hormone releasing hormone (LHRH) peptides that lead to suppression of LHRH activity in males or females. When male rats are immunized with these peptides, serum testosterone drops and androgen-dependent organs atrophy significantly. These peptides are useful for inducing infertility and for treating prostatic hyperplasia, androgen-dependent carcinoma, prostatic carcinoma and testicular carcinoma in males. In females, the peptides are useful for treating endometriosis, benign uterine tumors, recurrent functional ovarian cysts and (severe) premenstrual syndrome as well as prevention or treatment of estrogen-dependent breast cancer. The subject peptides contain a helper T cell epitope and have LHRH at the C terminus. The helper T cell epitope aids in stimulating the immune response against LHRH. The peptides, optionally contain an invasin domain which acts as a general immune stimulator. In another aspect this invention relates to immunogenic synthetic peptides having an invasin domain, a helper T cell epitope and a peptide hapten and methods of using these peptides to treat disease or provide protective immunity. The peptide haptens of the invention include LHRH, amylin, gastrin, gastrin releasing peptide, IgE CH4 peptide, Chlamydia MOMP peptides, HIV V3 peptides and Plasmodium berghei.

US PAT NO: 5,739,106 [IMAGE AVAILABLE] L3: 3 of 18
TITLE: Appetite regulating compositions
INVENTOR: Timothy J. Rink, 6041 Camino De La Costa, La Jolla, CA 92037
Andrew A. Young, 510 Josh Way, Alpine, CA 91901
Nigel Robert Arnold Beeley, 227 Loma Corta Dr., Solana Beach, CA 92037
Kathryn S. Prickett, 7612 Trailbrush Ter., San Diego, CA 92126
DATE FILED: Jun. 7, 1995
US-CL-CURRENT: 514/12, 16, 18, 19; 530/303, 307, 312, 324, 328, 331

ABSTRACT:
Compositions and methods for reducing food intake, suppressing appetite and controlling body weight are provided. Such compositions may include an amylin agonist and a CCK agonist or a hybrid peptide.

US PAT NO: 5,67[redacted]279 [IMAGE AVAILABLE] [redacted] L3: 4 of 18
TITLE: Methods and compositions for treating pain with amylin or agonists thereof
INVENTOR: Andrew A. Young, San Diego, CA
DATE FILED: Dec. 16, 1996
US-CL-CURRENT: 514/12

ABSTRACT:
Methods for treating pain are disclosed which comprise administration of a therapeutically effective amount of an amylin or an amylin agonist alone or in conjunction with a narcotic analgesic or other pain relief agent.

US PAT NO: 5,625,032 [IMAGE AVAILABLE] L3: 5 of 18
TITLE: Selective amylin antagonist peptides and uses therefor
INVENTOR: Lori Gaeta, Olivenhain, CA
Kevin Beaumont, San Diego, CA
Kathryn Prickett, San Diego, CA
DATE FILED: Jul. 21, 1993
US-CL-CURRENT: 530/324, 325, 326

ABSTRACT:
Peptides that inhibit amylin activity and that exhibit selectivity for amylin receptors relative to calcitonin and CGRP receptors are provided. These peptides may be used in the treatment of conditions where it is of benefit to reduce amylin activity, including the treatment of Type 2 diabetes mellitus, impaired glucose tolerance, obesity, insulin resistance and hypertension.

US PAT NO: 5,599,841 [IMAGE AVAILABLE] L3: 6 of 18
TITLE: Use of 3-guanidinopropionic acid in the treatment and prevention of metabolic disorders
INVENTOR: Martin D. Meglasson, Kalamazoo, MI
DATE FILED: Aug. 2, 1993
US-CL-CURRENT: 514/557, 565, 634

ABSTRACT:
The present invention provides a method for treating or preventing certain metabolic disorders comprising the systemic administration of 3-guanidinopropionic acid.

US PAT NO: 5,580,953 [IMAGE AVAILABLE] L3: 7 of 18
TITLE: Amylin antagonist peptides and uses therefor
INVENTOR: Elisabeth Albrecht, San Diego, CA
Howard Jones, Poway, CA
Laura S. L. Gaeta, La Jolla, CA
Kathryn S. Prickett, San Diego, CA
Kevin Beaumont, San Diego, CA
DATE FILED: Nov. 19, 1991
US-CL-CURRENT: 530/303, 324

ABSTRACT:
Compounds which inhibit amylin activity are provided. These compounds may be used in the treatment of conditions where it is of benefit to reduce amylin activity, including the treatment of Type 2 diabetes mellitus, impaired glucose tolerance, obesity and insulin resistance.

US PAT NO: 5,424,394 [IMAGE AVAILABLE] L3: 8 of 18
TITLE: Synthetic preparation of amylin and amylin analogues
INVENTOR: Laura S. Lehman de Gaeta, 8126 Camino del Sol, La Jolla, CA 92037
Elisabeth Albrecht, 10540 Bannister Way, San Diego, CA 92126
DATE FILED: Jul. 8, 1993

US-CL-CURRENT: 530/[redacted], 307, 327

ABSTRACT:
Synthetic amylin and amylin analogs which have high biological activity and which are substantially free from deletion peptides and other contaminating peptides are provided. Also provided are methods for the solid phase peptide synthesis of amylin and amylin analogs.

US PAT NO: 5,405,831 [IMAGE AVAILABLE] L3: 9 of 18
TITLE: Treatment of bone disorders
INVENTOR: Iain MacIntyre, Heathfield, England
DATE FILED: Jul. 27, 1993
US-CL-CURRENT: 514/4, 12; 530/303, 307, 324

ABSTRACT:
Use of amylin, or variants of amylin, as well as amylin agonists, for the treatment of bone disorders, in particular osteoporosis, Paget's disease, and malignant deposits in bone, bone loss of malignancy or endocrine disorders or autoimmune arthritides or immobility and disuse, and in other conditions where a hypocalcaemic effect is of benefit. Functional peptide fragments of amylin, or a variant of amylin or amylin fragment, are provided as well as a soluble amylin, amylin fragments, or variants thereof, or a lyophilized product, or an oral formulation for use alone, or in combination with other agents, including insulin (or insulin-stimulating agents, including but not limited to the sulfonylureas) and estrogens, for the treatment of disorders of bone or calcium balance.

US PAT NO: 5,376,638 [IMAGE AVAILABLE] L3: 10 of 18
TITLE: Methods for treating renin-related disorders with amylin antagonists
INVENTOR: Andrew A. Young, San Diego, CA
Timothy J. Rink, La Jolla, CA
DATE FILED: Sep. 1, 1992
US-CL-CURRENT: 514/12, 11, 13

ABSTRACT:
Methods for treating conditions associated with elevated, inappropriate or undesired renin activity are disclosed which comprise administration of an effective amount of any amylin antagonist alone or in conjunction with other anti-hypertensive agents. Methods for screening for and/or evaluating anti-renin amylin antagonists are also described.

US PAT NO: 5,364,841 [IMAGE AVAILABLE] L3: 11 of 18
TITLE: Treatment of obesity and essential hypertension and related disorders
INVENTOR: Garth J. S. Cooper, Solana Beach, CA
Brendan Leighton, Eynsham, England
DATE FILED: Jun. 21, 1993
US-CL-CURRENT: 514/12, 4, 13, 14, 15, 16, 17

ABSTRACT:
The administration of antagonists and blockers of amylin or CGRP or both for the treatment of obesity and essential hypertension and associated lipid disorders and atherosclerosis.

US PAT NO: 5,280,014 [IMAGE AVAILABLE] L3: 12 of 18
TITLE: Treatment of obesity and essential hypertension and related disorders
INVENTOR: Garth J. S. Cooper, Solana Beach, CA
Brendan Leighton, Eynsham, England
DATE FILED: Jul. 18, 1991
US-CL-CURRENT: 514/12, 4, 13, 14, 15, 16, 17

ABSTRACT:

The administration [redacted] antagonists and blockers of am[redacted]in or CGRP or both for the treatm[redacted]t of obesity and essential hype[redacted]nsion and associated lipid disorders and atherosclerosis.

US PAT NO: 5,266,718 [IMAGE AVAILABLE] L3: 13 of 18
TITLE: Ethanolamine benzoate compounds
INVENTOR: Michel Wierzbicki, L'Etang la Ville, France
Pierre Hugon, Rueil Malmaison, France
Jacques Duhault, Croissy sur Seine, France
Francoise Lacour, Vincennes, France
Michelle Boulanger, Marly le Roi, France
DATE FILED: Jun. 12, 1992
US-CL-CURRENT: 560/36, 37, 106

ABSTRACT:
New ethanolamine benzoate compounds which can be used as medicaments and correspond to the formula: ##STR1## wherein R is as defined in the description, in the form of racemic compounds and enantiomers. These new compounds and their physiologically tolerable salts can be used therapeutically for treatment of insulin-resistance states.

US PAT NO: 5,266,591 [IMAGE AVAILABLE] L3: 14 of 18
TITLE: Ethanolamine benzoate compounds
INVENTOR: Michel Wierzbicki, L'Etang La Ville, France
Pierre Hugon, Rueil Malmaison, France
Jacques Duhault, Croissy Sur Seine, France
Michelle Boulanger, Marly Le Roi, France
Francoise Lacour, Vincennes, France
DATE FILED: Nov. 20, 1992
US-CL-CURRENT: 514/539, 540; 560/36, 37, 41

ABSTRACT:
The compounds are ethanolamine benzoate compounds useful for the treatment of syndrome X, and of hypertension in patients who are insulin resistant or have one or more metabolic anomalies.
A compound disclosed is S-1-(m-trifluoromethylphenyl)-2-{.beta.-{4-[2-(N-(3,3-diphenylpropionyl)amino)ethyl] benzoyloxy}ethylamino} propane.

US PAT NO: 5,260,275 [IMAGE AVAILABLE] L3: 15 of 18
TITLE: Hypoglycemics
INVENTOR: Garth J. S. Cooper, Solana Beach, CA
Candace X. Moore, San Diego, CA
DATE FILED: Aug. 14, 1990
US-CL-CURRENT: 514/12, 13, 866

ABSTRACT:
Non-insulin dependent, or type 2, diabetes mellitus in a patient is treated by administering to the patient a hypoglycemic agent that enhances plasma concentrations of amylin and a therapeutically effective amount of an amylin antagonist. Hypoglycemic agents which enhance plasma concentrations of amylin can be sulfonylureas such as glibenclamide and tolbutamide. Amylin antagonists can be amylin 8-37 and CGRP 8-37. Administration of the amylin antagonist in conjunction with the hypoglycemic agent also enhances the blood glucose lowering effects of the hypoglycemic agent.

US PAT NO: 5,234,906 [IMAGE AVAILABLE] L3: 16 of 18
TITLE: Hyperglycemic compositions
INVENTOR: Andrew Young, San Diego, CA
Garth J. S. Cooper, Solana Beach, CA
DATE FILED: Jan. 10, 1991
US-CL-CURRENT: 514/12, 21

ABSTRACT:
Compositions having amylin or an amylin agonist and a glucagon compound,

particularly peptide compounds, for the control of glucose production in mammals are provided. The compositions are useful in the treatment of hypoglycemia, including acute hypoglycemic conditions such as those brought on by insulin overdose and the overuse of oral hypoglycemic agents.

US PAT NO: 5,134,164 [IMAGE AVAILABLE] L3: 17 of 18
TITLE: Use of 3-guanidinopropionic acid in the treatment of excess adiposity
INVENTOR: Martin D. Meglasson, Kalamazoo, MI
DATE FILED: Aug. 14, 1991
US-CL-CURRENT: 514/565, 557, 634

ABSTRACT:
The present invention provides a method for treating or preventing certain metabolic disorders comprising the systemic administration of 3-guanidinopropionic acid.

US PAT NO: 5,132,324 [IMAGE AVAILABLE] L3: 18 of 18
TITLE: Use of 3-guanidinopropionic acid in the treatment of non-insulin dependent diabetes mellitus (NIDDM)
INVENTOR: Martin D. Meglasson, Kalamazoo, MI
DATE FILED: Jun. 10, 1991
US-CL-CURRENT: 514/565, 557, 634, 866

ABSTRACT:
The present invention provides a method for treating or preventing certain metabolic disorders comprising the systemic administration of